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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/360,685	07/26/1999	ANTONELLO COVACCI	CHIR-0157	4520

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/360,685	COVACCI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *40,41 and 127* is/are allowed.

6)☒ Claim(s) *45,54,57,59,62,63,70,78,80,81,88,123,126,128 and 140-180* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 40,41,45,54,57,59,62,63,68,70,78,80,81,88,123,126-128 and 140-180.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 09/10/04 in response to the non-final Office Action mailed 06/10/04.

Status of Claims

2) Claims 45, 54, 57, 59, 62, 63, 70, 78, 80, 81, 123, 126 and 140 have been amended via the amendment filed 09/10/04.

Claims 47, 56, 124 and 125 have been canceled via the amendment filed 09/10/04.

New claims 141-180 have been added via the amendment filed 09/10/04.

Claims 40, 41, 45, 54, 57, 59, 62, 63, 68, 70, 78, 80, 81, 88, 123, 126-128 and 140-180 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the specification made in paragraph 6 of the Office Action mailed 06/10/04 with regard to the new matter, is withdrawn in light of Applicants' explanation.

Rejection(s) Moot

6) The rejection of claims 124 and 125 made in paragraph 19 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924), is moot in light of Applicants' cancellation of the claims.

7) The rejection of claims 47 and 56 made in paragraph 13 of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claims.

8) The rejection of claims 124 and 125 made in paragraph 14 of the Office Action mailed

06/10/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claims.

9) The rejection of claims 47, 56, 124 and 125 made in paragraph 20 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(b) as being anticipated by Covacci *et al.* (*PNAS* 90: 5791-5795, June 1993 - Applicants' IDS), is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

10) The rejection of claims 45, 54, 62, 68, 78, 81 and 88 made in paragraph 13 of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claims.

11) The rejection of claim 123 made in paragraph 14 of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claims 57, 59, 63 and 140 made in paragraph 15(b) of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

13) The rejection of claims 70, 80 and 126 made in paragraph 15(c) of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

14) The rejection of claim 57 made in paragraph 15(d) of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claim.

15) The rejection of claim 128 made in paragraph 15(e) of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the base claim.

16) The rejection of claims 81 and 88 made in paragraph 17 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(b) as being anticipated by Peterson *et al.* (*Nature* 354: 369-373, 1991, already of record), is withdrawn in light of Applicants' amendments to the claims.

17) The rejection of claims 81 and 88 made in paragraph 18 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(b) as being anticipated by Guntaka *et al.* (*Biochem. Biophys. Res.*

Commun. 182: 412-419, 1992), is withdrawn in light of Applicants' amendments to the claims.

18) The rejection of claim 123 made in paragraph 19 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924), is withdrawn in light of Applicants' amendment to the claim.

19) The rejection of claims 57, 59, 70 and 80 made in paragraph 21 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(e)(2) as being anticipated by Figura *et al.* (US 5,900,372, filed 10/16/1992) ('372) as evidenced by Figura *et al.* (US 5,866,375) ('375), is withdrawn in light of Applicants' amendments to the claims and/or the base claim(s).

20) The rejection of claim 63 made in paragraph 22 of the Office Action mailed 06/10/04 under 35 U.S.C. § 103(a) as being unpatentable over Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924) and Dunn *et al.* (*Infect. Immun.* 60: 1946-1951, May 1992 - Applicants' IDS) or Evans *et al.* (*Infect. Immun.* 60: 2125-2127, May 1992 - Applicants' IDS) in view of Hirschl *et al.* (*In*: *Helicobacter pylori, gastritis and peptide ulcer.* (Ed) Malfertheiner et al. Springer-Verlag, Berlin Heidelberg, 141-146, 1990) (not *Eur. J. Clin. Microbiol. Infect. Dis.* 7: 100-105, 1988 as cited inadvertently in the last Office Action), is withdrawn in light of Applicants' amendment to the claim.

21) The rejection of claim 140 made in paragraph 23 of the Office Action mailed 06/10/04 under 35 U.S.C. § 103(a) as being unpatentable over Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924) and Cover *et al.* (US 6,054,132, filed 02/26/1992) ('132) in view of Hirschl *et al.* (not *Eur. J. Clin. Microbiol. Infect. Dis.* 7: 100-105, 1988 as cited inadvertently in the last Office Action), is withdrawn in light of Applicants' amendment to the claim.

Rejection(s) Maintained

22) The rejection of claim 57 made in paragraph 15(a) of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein and herebelow.

Applicants state that they have amended the claim to recite the open-ended term 'comprising' which would make it clear to one of ordinary skill in the art that a polypeptide comprising at least ten contiguous amino acids may have more than ten contiguous amino acids, for example, SEQ ID NO: 9.

Applicants' argument has been carefully considered, but is non-persuasive. The claim is

still confusing. One of skill in the art can make out how a ten amino acid-long polypeptide 'comprises' a six amino acid-long NNNNNN amino acid sequence within it. However, as set forth previously, it is unclear how a polypeptide having the minimally required length of 10 contiguous amino acids can comprise within it an amino acid sequence that is longer than 10 contiguous amino acids in length. The claim is internally inconsistent. A ten amino acid-long polypeptide cannot comprise within it a twelve amino acid-long fragment or polypeptide.

23) The rejection of claim 59 made in paragraph 15(e) of the Office Action mailed 06/10/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein.

New claims 164-166, which depend from claim 57, are now included in this rejection and are viewed as being indefinite because of the indefiniteness identified above in the base claim 57.

24) The rejection of claims 126 and 128 made in paragraph 19 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924), is maintained for reasons set forth therein and herebelow.

Applicants state that claims as amended are entitled to priority over the '924 patent because Figure 3B and 3C and claims 2 and 3 of the Italian priority document, FY92A/000052, is entitled to a priority date of 2 March 1992.

Applicants' argument has been carefully considered, but is not persuasive. The base claim 126, as amended, requires the CAI antigen having the amino acid sequence of SEQ ID NO: 5 to be encoded by fifteen contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 4. However, such limitations are not supported in the Italian priority document, FY92A/000052, or in the instant application. Therefore, Cover's ('924) patent still applies as prior art.

25) The rejection of claims 45, 54, 62, 68, 78, 81, 88, 123 and 128 made in paragraph 20 of the Office Action mailed 06/10/04 under 35 U.S.C. § 102(b) as being anticipated by Covacci *et al.* (*PNAS* 90: 5791-5795, June 1993 - Applicants' IDS), is maintained for reasons set forth therein and herebelow. Claim 126 is now included in this rejection.

Applicants contend that the disclosure of amino acids 750-977 of SEQ ID NO: 5 and nucleotides 2782-3466 of SEQ ID NO: 4 in Figures 3B and 3C and claims 2 and 3 of the Italian Priority document, FI92A/000052, is entitled to a priority date of 02 March 1992, and therefore

'Cover patent' should not qualify as prior art.

Applicants' argument has been carefully considered, but is non-persuasive. The reference of Covacci *et al.* qualifies as prior art because the instant claims are not granted priority to the Italian priority application. See the new matter rejections made below for an explanation.

Rejection(s) under 35 U.S.C § 101

26) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

27) Claims 54 and 141-152 are rejected under 35 U.S.C § 101 as being directed to a non-statutory subject matter.

Claim 54 and new claims 141-152 do not sufficiently distinguish over a naturally occurring polypeptide(s) of *H. pylori* as it exists naturally, for example, on the surface of *H. pylori*, because the claims do not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980)*. The base claim(s) should be amended to indicate the hand of the inventor, e.g., by insertion of '--an isolated polypeptide--, or --a purified polypeptide--, if descriptive support exists for such a limitation in the instant application. See MPEP 2105.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

28) Claims 45, 54, 62 and 81 and claims 68, 78 and 88 dependent therefrom, and new claims 141, 142, 147, 154, 159 and those dependent therefrom, are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Instant claims include the limitations: 'polypeptide compris... amino acids 750-977 of the amino acid sequence of SEQ ID NO: 5'. The recited polypeptide encompasses: (a) a polypeptide comprising amino acids 750-977 of SEQ ID NO: 5 and one or more of any other amino acids on either side of amino acids 750-977; and (b) a full length polypeptide comprising the amino acid sequence of SEQ ID NO: 5. However, there appears to be no descriptive support in the

specification, as originally filed, for such a scope. Furthermore, the limitation '750-977' is absent in the instant application. The limitations '750-977' and 'SEQ ID NO: 5' are both absent in the Italian priority application. Figure 4 of the instant application does not indicate amino acids 750-977 of the amino acid sequence of SEQ ID NO: 5 to be separable from the whole sequence either by underlining or boxing the specifically recited amino acids within SEQ ID NO: 5. It does not appear that amino acids 750-977 of the amino acid sequence of SEQ ID NO: 5 are recited or identified separately as a fragment of SEQ ID NO: 5 either in the raw sequence listing or in any part of the specification. Figure 3C of the Italian priority document does not depict the polypeptide of SEQ ID NO: 5. Figure 3C of the priority document is not described as depicting a polypeptide fragment that is separable from the instantly recited SEQ ID NO: 5. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

29) Claim 123 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 123, as amended, includes the limitations: polypeptide encoded by 'a polynucleotide sequence comprising' nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4. The recited polynucleotide encompasses: (a) a polynucleotide comprising nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4 and one or more of any other nucleotides on either side of nucleotides 2782-3466; and (b) the full length polynucleotide comprising the whole nucleotide sequence of SEQ ID NO: 4. Because of the newly introduced open claim language 'comprising', the full length polynucleotide comprising the whole nucleotide sequence of SEQ ID NO: 4 is not excluded from the scope of the claim. However, there appears to be no descriptive support in the specification, as originally filed, for such a scope. Furthermore, the limitation '2782-3466' is absent

in the instant application. The limitations '2782-3466' and 'SEQ ID NO: 4' are absent in the Italian priority application. Figure 4 of the instant application does not indicate nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4 to be separable from the whole sequence either by underlining or boxing the specifically recited nucleotides. It does not appear that nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO: 4 are recited or identified separately as a fragment of SEQ ID NO: 4 either in the raw sequence listing or in any part of the specification. Figure 3B of the Italian priority document does not depict the nucleotide sequence of SEQ ID NO: 4. Figure 3B of the priority document is not described as depicting a nucleotide sequence fragment that is separable from the instantly recited SEQ ID NO: 4. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C § 112, Second Paragraph

30) Claims 63, 70, 80, 126, 128, 140, 156-158 and 164-180 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 126 is confusing and internally inconsistent in the limitations: 'immunogenic polypeptide ..... comprising CAI .. antigen having the amino acid sequence of SEQ ID NO. 5, wherein said polypeptide is encoded by at least fifteen contiguous nucleotides of the nucleotide sequence of SEQ ID NO. 4'. The limitation 'at least fifteen contiguous nucleotides of .... SEQ ID NO: 4' encompasses 15, 20, 25, 30 etc. nucleotides of SEQ ID NO: 4. It is unclear how a polypeptide comprising the whole CAI antigen having the amino acid sequence of SEQ ID NO: 5 can be encoded by 15, 20, 25, or 30 contiguous nucleotides of SEQ ID NO: 4.

(b) Claim 128, which depends from claim 126, is indefinite because of the indefiniteness identified above in the base claim.

(c) Claims 156-158 are vague, indefinite and incorrect in the limitation: 'immunogenic

composition of claim 154', because claim 154 is drawn to a method and not to an immunogenic composition.

(d) Claims 164-166 are rejected as being indefinite because of the indefiniteness identified above in the base claim 57. See paragraph 23 above.

(e) Claims 63, 70, 170, 172 and 176 are indefinite, confusing and/or internally inconsistent in the recitation: 'at least ten contiguous amino acids of the amino acid sequence of SEQ ID NO: 5, wherein said polypeptide comprises ..... SEQ ID NO: 9'. The minimum length requirement of the claimed polypeptide is ten contiguous amino acids of the amino acid sequence of SEQ ID NO: 5, and it is required to include SEQ ID NO: 9. However, SEQ ID NO: 9 is longer than ten contiguous amino acids in length. It is unclear how a longer than ten contiguous amino acid-long polypeptide can be contained in a ten contiguous amino acid-long polypeptide.

(f) Claims 80, 140, 167-169, 171, 173-175 and 177-180 are rejected as being indefinite because of the indefiniteness identified above in the base claim 63, 70, 170, 172 or 176.

Rejection(s) under 35 U.S.C § 102

31) Claims 54, 81, 88, 123, 126, 128 and 141-152 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Figura *et al.* (US 5,900,372, filed 10/16/1992 – already of record) ('372) as evidenced by Figura *et al.* (US 5,866,375 – already of record) ('375).

It is noted that the polypeptide comprising the recited number(s) of amino acids of SEQ ID NO: 5, with or without the amino acid sequence of SEQ ID NO: 6 or SEQ ID NO: 3, as claimed in claims 54 and 141-152, is neither required to be isolated, nor purified. The polypeptide comprising the recited number of amino acids of SEQ ID NO: 5 as claimed in claims 81 and 123 is not required to be purified.

Figura *et al.* ('372) disclosed a composition comprising bacterial cells; a supernatant of treated and centrifuged bacterial cells (i.e., isolated); and a bacterial cell layer extracted from the CCUG 17874 cytotoxic strain of *H. pylori* contained in phosphate buffer (i.e., pharmaceutically acceptable carrier), which comprise the 130 kD cytotoxic and vacuolating protein as well as other proteins of *H. pylori*. A method of bringing the bacterial cells or the cell layer preparation into association with a buffer is taught, which method inherently involves the combining of cytotoxin or HSP with vacuolating protein, since the bacterial cells and the cell layer preparation of the *H. pylori*

strain CCUG 17874 are expected to contain all these proteins. See Example 3, lines 7-9; Example 2; the second full paragraph in column 2; and Figures 1 and 2. That the prior art 130 kD protein is the 128 kD cytotoxin-associated protein and the 90 kD protein is the immunoprotective VacA protein is inherent from the teachings of Figura *et al.* in light of what was known in the art at the time. For instance, Figura *et al.* ('375) described these proteins as such. See column 2, first full paragraph; Figures 1, 2 and 4, and their descriptions; first paragraph of Examples 3 and 7; Examples 8 and 9; and claims. Although Figura *et al.* ('372) are silent about the SEQ ID number(s) as recited and the nucleotides encoding the same, since the prior art polypeptides are produced by the same CCUG 17874 strain of *H. pylori* as that of Applicants' strain (see sections 'Materials and methods' and 'Results' of the instant specification), the prior art composition is expected to have the same structure as recited, absent evidence to the contrary.

The limitation 'recombinant' in the instant claims is viewed as a process limitation in product claims. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art.

Claims 54, 81, 88, 123, 126, 128 and 141-152 are anticipated by Figura *et al.* ('372). The reference of Figura *et al.* ('375) is **not** used as a secondary reference in combination with Figura *et al.* ('372), but rather is used to show that every element of the claimed subject matter is disclosed by Figura *et al.* ('372). See *In re Samour* 197 USPQ 1 (CCPA 1978).

32) Claims 170 and 171 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988).

Instant claims are not granted priority to the foreign priority document since polypeptide fragments comprising SEQ ID NO: 9, SEQ ID NO: 10, or six contiguous asparagines residues lack descriptive support therein.

Cover *et al.* ('924) disclosed a method of bringing a purified 120-128 kilodalton polypeptide into association with a pharmaceutically acceptable carrier. Cover's ('924) polypeptide comprises at least ten contiguous amino acids of the instantly recited amino acid sequence of SEQ ID NO: 5 and recombinant fragments thereof. See abstract; paragraph bridging columns 3 and 4; and first two paragraphs in column 4. The prior art polypeptide comprises Glu Phe Lys Asn Gly Lys Asn Lys Asp Phe Ser Lys Val Thr Gln Ala Lys Ser Asp residues which constitutes an at least ten contiguous amino acid residue-long fragment of the instantly claimed SEQ ID NO: 5 (see columns 31 and 32 of the '924 patent) and includes the instantly recited SEQ ID NO: 9, i.e., EFKNGKNKDFSK. The purified polypeptide fragments are used, in immunogenically effective amounts, as vaccines along with a pharmaceutically acceptable carrier (see fifth full paragraph in column 3; and section 'Vaccines' in column 10). Thus, a method of bringing the polypeptide into association with a pharmaceutically acceptable carrier is inherently disclosed. See the sequence search report attached to the Office Action mailed 05/20/03; and columns 31 and 32 of the '924 patent. The prior art polypeptide is long enough to be immunogenic, since it is well known in the art that the smallest peptides which elicit antibodies that bind to the original full length protein are six amino acids in length. See the first sentence under 'Size of the Peptide' on page 76 of Harlow *et al.*

Claims 170 and 171 are anticipated by Cover *et al.* ('924).

Rejection(s) under 35 U.S.C § 103

33) Claims 57, 59, 63, 140, 172-174 and 180 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924) and Dunn *et al.* (*Infect. Immun.* 60: 1946-1951, May 1992 - Applicants' IDS) or Evans *et al.* (*Infect. Immun.* 60: 2125-2127, May 1992 - Applicants' IDS) in view of Hirschl *et al.* (*In: Helicobacter pylori, gastritis and peptic ulcer.* (Ed) Malfertheiner et al. Springer-Verlag, Berlin Heidelberg, 141-146, 1990).

Instant claims are not granted priority to the foreign priority document since polypeptide fragments comprising SEQ ID NO: 9, SEQ ID NO: 10, or six contiguous asparagines residues lack descriptive support therein.

Cover *et al.* ('924) disclosed a method of bringing a purified 120-128 kilodalton polypeptide into association with a pharmaceutically acceptable carrier to produce an immunogenic composition. Cover's ('924) polypeptide comprises at least ten or fifteen contiguous amino acids of the instantly recited amino acid sequence of SEQ ID NO: 5 and recombinant fragments thereof. See abstract; paragraph bridging columns 3 and 4; and first two paragraphs in column 4. The prior art polypeptide comprises Glu Phe Lys Asn Gly Lys Asn Lys Asp Phe Ser Lys Val Thr Gln Ala Lys Ser Asp residues, which constitutes an at least ten or fifteen contiguous amino acid residue-long fragment of the instantly claimed SEQ ID NO: 5 (see columns 31 and 32 of the '924 patent) and includes the instantly recited SEQ ID NO: 9, i.e., EFKNGKNKDFSK. The purified polypeptide fragments are used, in immunogenically effective amounts, as vaccines along with a pharmaceutically acceptable carrier (see fifth full paragraph in column 3; and section 'Vaccines' in column 10). Thus, a method of bringing the polypeptide into association with a pharmaceutically acceptable carrier is inherently disclosed. See the sequence search report attached to the Office Action mailed 05/20/03; and columns 31 and 32 of the '924 patent.

The teachings of Cover *et al.* ('924) are disclosed *supra*, which do not disclose the step of adding a second polypeptide comprising at least ten contiguous amino acids of *H. pylori* heat shock protein having the amino acid sequence of SEQ ID NO: 6.

However, Dunn *et al.* taught an intrinsically immunogenic heat shock protein of *H. pylori* comprising at least ten or fifteen contiguous amino acids, from position 2-34 of the instantly recited SEQ ID NO: 6, AKEIKFSDSARNLLFEGVRQLHDAVKVTMGFRG, which protein is isolated and/or purified from the water extract of whole cells or culture supernatants (see Figure 2 and pages 1948-1950).

Similarly, Evans *et al.* taught a purified heat shock protein of *H. pylori* comprising an N-terminal sequence at least ten or fifteen contiguous amino acids in length, AKEIKFSDSARNLLFEGVRQLHDAVKVTMGFRG, from position 2-34 of the instantly recited SEQ ID NO: 6 (see Table 1; and abstract). Evans' protein is long enough to be immunogenic.

Hirschl *et al.* taught a highly purified *H. pylori* protein antigen with a molecular weight of approximately 120 kDa (see paragraph bridging pages 143 and 144 and Table 3). Hirschl *et al.* taught 'unicomponent antigens' of *H. pylori* such as the 120 kDa protein and 'multicomponent'

purified antigens, such as, the acid-glycine extract. Hirschl *et al.* taught a purified urease antigen of *H. pylori*. Hirschl *et al.* expressly taught mixing or combining various *H. pylori* antigens with the 120 kDa *H. pylori* antigen for use in serodiagnostic tests such as ELISA (see page 144; page 142 and Tables 3 and 4).

Given Hirschl's express disclsoure of combining or mixing various *H. pylori* antigens, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Evans' or Dunn's intrinsically immunogenic heat shock protein of *H. pylori* to Cover's ('924) composition and thus provide the step of adding the *H. pylori* heat shock protein in Cover's ('924) method to produce the method and the composition of the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a method of producing a multicomponent antigen composition for use in serodiagnostic tests to diagnose *H. pylori* infections as taught by Hirsch *et al.*

The limitation 'recombinant' in claims 173, 174 and 180 is viewed as a process limitation in product claims. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art polypeptide differs from that of the instantly recited second polypeptide.

Claims 57, 59, 63, 140, 172-174 and 180 are *prima facie* obvious over the prior art of record.

34) Claims 70, 80, 167, 168 and 176-178 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cover *et al.* (US 5,403,924 - Applicants' IDS) ('924) and Cover *et al.* (US 6,054,132, filed 02/26/1992) ('132) in view of Hirschl *et al.* (*In*: *Helicobacter pylori, gastritis and*

peptic ulcer. (Ed) Malfertheiner et al. Springer-Verlag, Berlin Heidelberg, 141-146, 1990).

Instant claims are not granted priority to the foreign priority document since polypeptide fragments comprising SEQ ID NO: 9, SEQ ID NO: 10, or six contiguous asparagines residues lack descriptive support therein.

Cover *et al.* ('924) disclosed a method of bringing a purified 120-128 kilodalton polypeptide into association with a pharmaceutically acceptable carrier to produce an immunogenic composition. Cover's ('924) polypeptide comprises at least ten or fifteen contiguous amino acids of the instantly recited amino acid sequence of SEQ ID NO: 5 and recombinant fragments thereof. See abstract; paragraph bridging columns 3 and 4; and first two paragraphs in column 4. The prior art polypeptide comprises Glu Phe Lys Asn Gly Lys Asn Lys Asp Phe Ser Lys Val Thr Gln Ala Lys Ser Asp residues which constitutes an at least ten or fifteen contiguous amino acid residue-long fragment of the instantly claimed SEQ ID NO: 5 (see columns 31 and 32 of the '924 patent) and includes the instantly recited SEQ ID NO: 9, i.e., EFKNGKNKDFSK. The purified polypeptide fragments are used, in immunogenically effective amounts, as vaccines along with a pharmaceutically acceptable carrier (see fifth full paragraph in column 3; and section 'Vaccines' in column 10). Thus, a method of bringing the polypeptide into association with a pharmaceutically acceptable carrier is disclosed. See the sequence search report attached to the Office Action mailed 05/20/03; and columns 31 and 32 of the '924 patent.

The teachings of Cover *et al.* ('924) are disclosed *supra*, which do not disclose the step of adding a second polypeptide comprising at least ten contiguous amino acids of *H. pylori* cytotoxin protein having the amino acid sequence of SEQ ID NO: 3.

However, Cover *et al.* ('132) taught a purified, immunogenic, recombinantly produced polypeptide of *H. pylori* comprising 23 contiguous amino acids, AFFTTVIIPAIVGGIATGTAVGT, of the instantly recited SEQ ID NO: 3 (see abstract; lines 29-47 of column 2; Example 2; Table 2 and SEQ ID NO: 13). The antigen is used for diagnostic purposes (see last paragraph in column 2).

Hirschl *et al.* taught a highly purified *H. pylori* protein antigen with a molecular weight of approximately 120 kDa (see paragraph bridging pages 143 and 144 and Table 3). Hirschl *et al.* taught 'unicomponent antigens' of *H. pylori* such as the 120 kDa protein and 'multicomponent' purified antigens, such as, the acid-glycine extract. Hirschl *et al.* taught a purified urease antigen of

H. pylori. Hirschl *et al.* expressly taught mixing or combining various *H. pylori* antigens with the 120 kDa *H. pylori* antigen for use in serodiagnostic tests such as ELISA (see page 144; page 142; and Tables 3 and 4).

Given Hirschl's express teaching of combining or mixing various *H. pylori* antigens, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Cover's ('132) purified immunogenic polypeptide of *H. pylori* to Cover's ('924) composition and thus provide the step of adding Cover's ('132) immunogenic polypeptide in Cover's ('924) method to produce the method and the composition of the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a method of producing a multicomponent antigen composition for use in serodiagnostic tests to diagnose *H. pylori* infections as taught by Hirsch *et al.*

Claims 70, 80, 167, 168 and 176-178 are *prima facie* obvious over the prior art of record.

Remarks

35) Claims 45, 54, 57, 59, 62, 63, 68, 70, 78, 80, 81, 88, 123, 126, 128 and 140-180 stand rejected. Claims 40, 41, and 127 are allowable.

36) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (703) 872-9306.

37) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

38) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may

be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

November, 2004

SD

S. DEVI, PH.D.
PRIMARY EXAMINER